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## REMARKS

After entry of this amendment, Claims 1-2, 4-13 are pending. Claim 1 has been amended and new claims, Claims 10-13, have been added. Support for the amendment and the new claims is found at least on page 4, lines 11-19. No new matter has been added.

Based on the following remarks, Applicant respectfully requests reconsideration and allowance of the pending claims.

Rejection of Claims 1, 2 and 4-9 under 35 U.S.C. §103(a)

The Examiner rejected Claims 1, 2 and 4-9 under 35 U.S.C. § 103(a) as being unpatentable over Sedlacek *et al.*, Int. J. Immunopharmacol., 9 (7), 1987, abstract [Sedlacek 1987]; Sedlacek, *et al.*, Cancer Immunol. Immunother. 23 (3), 1986, abstract [Sedlacek 1986]; Maiskii *et al.*, Byull eksp biol med (12) 1977 (recd 1978) abstract [Maiskii 1977]; Knop *et al.*, Immunology, 34 (2), 1978 abstract [Knop 1978]; Gautam *et al.*, Indian J. Med. Res 64 (3), 1976 abstract [Gautam 1976]; Sedlacek, *et al.*, Cancer Immunology Immunother 1978 5/3 abstract [Sedlacek 1978]; or Mobley *et al.*, Res. Commun. Chem. Path. Pharmacol. 1974, 9/1 abstract [Mobley 1974]; taken with Green *et al.*, Kline *et al.*, '133 or Kline *et al.*, '863. The Examiner stated that the references each teach that an animal with a tumor was injected with neuraminidase, that Green provides the teaching of a phenol-saline carrier and that the Kline patents teach administration by sublingual and nasal routes.

None of the cited references teach a method of treating neoplasms or cancer by the administration of a very small amount of neurominidase, of less than approximately $10^{-2}$ mg to approximately $10^{-8}$ mg. It is not obvious from the teachings of any of the references that neurominidase in these small amounts would have any effect at all.

Sedlaceck 1987 teaches that only a checkerboard vaccination program, in which increasing numbers of chemically-treated tumor cells were mixed with increasing milliUnits of neuraminidase, was effective in preventing metastasis of Lewis lung adenocarcinoma. A single composition of cells treated with neurominidase, or a single composition of cells and neurominidase had no effect at all on metastasis. The checkerboard vaccination or any combinations of cells and

neuraminidase were ineffective for preventing metasasis by two other types of cancer. There is no teaching or suggestion in Sedlaceck 1987 of administering a small amount of neurominidase. Additionally, Sedlaceck 1987 teaches that only a particular method is effective, a checkerboard vaccination that requires multiple combinations of cells and neuraminidase, for only one type of metastasis. Other metastases are not effected by any treatment with cells and neuraminidase. There is no teaching of administering neuraminidase without cells, and thus, Sedlacek 1987 alone or in combination with the other cited art, does not make Applicant's currently pending invention prima facie obvious.

Sedlacek 1986 teaches the method of Sedlacek 1987 abstract as applied to dogs. The same checkerboard vaccination method is taught and again, there is no teaching or suggestion of administering neuraminidase in small amounts. The summation of the article is that checkerboard vaccination appears to be an effective therapy when multiple compositions of differing amounts of tumor cells and neurominidase are used. Applicant's current invention does not comprise a method of checkerboard vaccination or compositions of tumor cells and neurominidase. Thus, Sedlacek 1986 abstract or in combination with the other cited art, does not make Applicant's currently pending invention prima facie obvious.

Maiskii 1977 teaches that injection of 50 units of vibrio neuraminidase twice a week for 3 months was "effective in the early stages of carcinogenesis". There is no teaching of the amount of neuraminidase injected, and thus, the reference provides no teaching or suggestion of Applicant's currently claimed method. In a review of the Sigma catalog for vibrio neuraminidase, such as that taught in Applicant's Example 1, the neuraminidase sold by Sigma has 8 to 24 units per mg of protein. If such a neurominidase were used in the Maiskii experiments, the reference teaches injecting a dose of 2.08 mg to 6.25 mg. This amount of neuraminidase is magnitudes in amount different from Applicant's currently claimed method, and in fact, teaches away from Applicant's currently claimed invention, by teaching large amounts of neurominidase may have some effect. Thus, Maiskii 1977 alone or in combination with the other cited art, does not make Applicant's currently pending invention prima facie obvious.

Knop 1978 does not provide any teaching for Applicant's currently claimed method for the treatment of humans with cancer. Knop 1978 makes a bare statement

that treatment of tumor cells with VCN increases their immunogenicity. There is no teaching or suggestion that these cells are related in any way to cancer in humans, that these cells were treated in any other way than *in vitro*, or that immunogenicity has any relation to treatment of cancer in humans. Other statements in Knop 1978 are directed to antibody production. There is no teaching or suggestion in Knop 1978 of Applicant's currently claimed invention of administering neurominidase for the treatment of the cancer. There is no sufficient teaching of any method in Knop such that alone, or in combination with the other cited references, Applicant's currently claimed invention is rendered obvious.

Gautam 1976 is not an enabling reference and does not provide enough of a teaching or suggestion of Applicant's currently claimed invention to render it obvious. Gautam 1976 teaches that neuraminidase-treated cells, not neuraminidase, prevented the appearance of tumors. Gautam 1976 also teaches that neuraminidase injected "directly into the tumor challenge site" delayed and arrested tumors. Applicant's currently claimed method does not include injection into a tumor challenge site. There is no teaching or suggestion in Gautam 1976 of Applicant's currently claimed invention, and no teaching that provides any direction for a method for the treatment of cancer in humans as is currently claimed. Gautam 1976, alone or in combination with the other cited references, is insufficient in its teaching to render Applicant's currently claimed invention obvious.

Sedlacek 1978, at best, provides a mere suggestion that the dose of neuraminidase injected directly in to a tumor may be important for the outcome of treatment. No dose or amount is taught or suggested. Additionally, Sedlacek 1978 teaches that tumor therapeutic effect depends on the dose of cells and amount of neuraminidase, and there are differing effects with different tumors and different adjuvant treatments, and these differences can be overcome by use of the checkerboard vaccination method. There is no teaching or suggestion in Sedlacek 1978 of Applicant's currently claimed method of administering very small amounts of neuraminidase for the treatment of cancer. Sedlacek 1978 is an abstract of a review which is directed to showing the efficacy of checkerboard vaccination, which does not provide a teaching or suggestion of Applicant's currently claimed invention, and alone or in combination with the other cited references, does not render Applicant's invention obvious.

Mobley 1974 teaches that the intraperitoneal injection of a combination of PHA and neuraminidase extended the life of mice with Ehrlich ascites tumors. Mobley 1974 also teaches that the role of neuraminidase is unclear and that the activity of the two agents does not "preclude an immunoregressive role for VCN [neuraminidase]". At its broadest interpretation, this is a mere suggestion to investigate the role of neuraminidase, and provides no teaching or suggestion of effective methods for the treatment of cancer in humans. There is no teaching or suggestion of effective amounts of neuraminidase or of any activity of neuraminidase alone. Mobley 1974, alone or in combination with the other cited references, does not provide a teaching or suggestion of Applicant's currently claimed invention that would render Applicant's invention obvious.

As stated by the Examiner in an earlier telephone conference, Green "was cited as a general teaching to show the wide use of phenol-saline as a solution for injection of biological materials into the body", and as such, does not, in combination with the cited references, result in a teaching that renders the currently pending claims obvious. The same is true for the Kline patents, which were cited for teaching administration routes, and in combination with the cited references, do not provide a teaching that renders the currently pending claims obvious. Applicant respectfully requests the Examiner to withdraw the rejection.

## MARKED COPY OF AMENDMENTS

Amendments in the Claims

In accordance with 37 C.F.R. § 1.121(c), the following version of the claims as rewritten by the foregoing amendment shows all the changes made relative to the previous version of the claim. Deletions are shown in [brackets] and additions are underlined.

1. (Thrice Amended) A method for treating a human with cancer, comprising administering to the human with cancer [a composition comprising an effective amount] between approximately $10^{-2}$ mg to approximately $10^{-8}$ mg of neuraminidase.

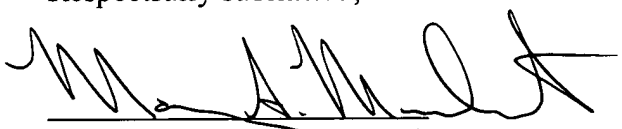
New Claims 10- 13.

## CONCLUSION

The foregoing is a complete response to the Office Action mailed December 19, 2002. Applicant respectfully submits that the present application is in condition for immediate allowance. An early notification is earnestly solicited. If the Examiner has any questions, or further issues remain to be resolved, the Examiner is requested to contact the undersigned at (404) 745-2426.

No additional fees are believed due; however, the Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, to Deposit Account No. 11-0855.

Respectfully submitted,



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